

PATENT SPECIFICATION

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The inventors of this invention in the sense of being the actual devisers thereof within the meaning of Section 16 of the Patents Act 1949 are WALTER SANNE, KARL-HEINZ KOENIG, ERNEST - HEINRICH POMMER and HERBERT STUMMEYER, citizens of Germany and residents, respectively, of 24 Ungsteiner Strasse, Ludwigshafen/Rhein, Germany; 40 Saarlandstrasse, Ludwigshafen/Rhein, Germany; 49 Bismarckstrasse, Ludwigshafen/Germany; and 19 Rethelstrasse, Mannheim, Germany.

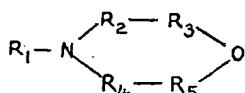
COMPLETE SPECIFICATION

N-substituted Morpholines having Fungicidal Activity

We, BADISCHE ANILIN- & SODA-FABRIK AKTIENGESELLSCHAFT, a German Joint Stock Company of Ludwigshafen / Rhein, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to fungicidal agents and methods of controlling fungi. More especially, the invention relates to agents and methods for controlling mildew.

We have found that good fungicidal activity is exhibited by compounds having the general formula



or salts or molecular or addition compounds thereof, in which formula R_1 denotes a cycloalkyl radical with more than 6 annular carbon atoms or a tridecyl- or an alkylphenyl radical, R_2 , R_3 , R_4 and R_5 may be identical or different, each denoting an unsubstituted or substituted methylene radical, the substituents being one or two methyl- and/or ethyl- and/or phenyl groups, with the proviso that, when R_1 represents a tridecyl- or alkylphenyl radical, at least one of the radicals R_2 , R_3 , R_4 and R_5 is a substituted methylene radical, the substituents being one or more methyl- and/or ethyl- and/or phenyl groups.

Suitable anions for salts are especially the anions of inorganic acids, for example hydrochloric acid, sulphuric acid, nitric acid, hydro-

bromic acid and phosphoric acid. Salts of organic acids are also suitable as active substances. By molecular or addition compounds we mean stoichiometrically substantially defined associations of molecules in the liquid or solid state which are caused by van der Waals forces (also dipolar orientation, hydrogen bonding and the like) and in the formation of which primary valences are neither dissolved nor freshly formed.

The active substances according to this invention may be prepared by methods which are analogous to conventional methods. For example they may be obtained by reaction of primary amines or alkanolamines with alkylene oxides to form dialkanolamines and cyclization of these compounds with dehydrating agents. Deydration may be carried out for example with concentrated sulphuric acid, hydrochloric acid or hydrobromic acid or dehydration catalysts, for example aluminum oxide, aluminum phosphate, or boron phosphate, in the liquid phase or in the gas phase.

Another method of preparation is hydrogenating amination of ketones with primary amino alcohols to form N - substituted alkanolamines which are then reacted with alkylene oxides as above described. The dialkanolamines are cyclized to a heterocyclic ring in the way already described with dehydrating agents.

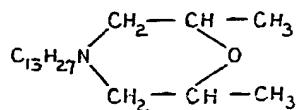
Moreover 2,2¹ - dichloroalkyl ethers, which may be substituted, may be reacted with primary amines in the presence of acid-binding agents to form compounds having a heterocyclic ring.

Morpholine salts are obtained from N-substituted dialkanolamines with thionyl halides.

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The compounds may be prepared according to the following specification:

500 parts (by weight) of concentrated sulphuric acid is allowed to flow into 531 parts of N - di - (2 - hydroxypropyl) - tridecylamine with stirring. Stirring is continued while the mixture is kept at 160°C. for an hour under a water jet vacuum. The mixture is then slowly added to 2500 parts of 25% caustic soda solution while stirring, allowed to settle and the upper layer (371 parts) separated off and dried over 50 parts of 50% caustic soda solution. The oily layer is separated off and distilled under reduced pressure. The boiling point of the product is 130° to 133°C. at 0.7 mm Hg. The yield is 331 parts of 2,6 - dimethyl - 4 - tridecylmorpholine, that is 66% of the theory with reference to N - di - (2 - hydroxypropyl)-tridecylamine. The compound has the following constitutional formula:



The salts may be prepared in conventional manner by mixing the initial materials, if desired in the presence of solvents. When pure initial materials are used, the salts, molecular compounds and addition compounds obtained usually do not need any further purification. Salts of organic acids (for example acetic acid, butyric acid, stearic acid, oxalic acid, adipic acid, maleic acid, lactic acid, tartaric acid, citric acid and trichloroacetic acid) are usually difficultly crystallisable viscous substances at room temperature. Salts of inorganic acids are usually amenable to crystallization. Some of them are hygroscopic.

Some of the active substances which may be used according to this invention are set out in the following Table by way of example:

N - cyclooctylmorpholine b.p.₁ 116°C. n_D²⁵ = 1.4950
 N - cyclooctylmorpholine hydrobromide m.p. 226° to 227°C.
 45 N - cyclooctyl - 2,6 - dimethylmorpholine b.p._{0.5} 103°C. n_D²⁵ 1.4855
 N - cyclooctyl - 2,6 - dimethylmorpholine hydrochloride m.p. 209°C. to 210°C. (with decomposition)
 50 N - cyclooctyl - 2,2,6,6 - tetramethylmorpholine (b.p._{0.5} 113°C.; n_D²⁵ = 1.4850)
 N - cyclooctyl - 2,6 - diethylmorpholine (b.p._{0.4} 124° to 125°C.; n_D²⁵ = 1.4850)
 55 N - cyclooctyl - 2 - methyl - 6 - ethylmorpholine (b.p._{0.5} 118°C.; n_D²⁵ = 1.4872)
 N - cyclooctyl - 2 - methyl - 6,6 - dimethylmorpholine (b.p._{0.5} 110°C.; n_D²⁵ = 1.4820)

N - cyclooctyl - 2 - methylmorpholine (b.p. _{0.5} 106°C.; n _D ²⁵ = 1.4920)	60
N - cyclooctyl - 2,2 - dimethylmorpholine (b.p. _{0.2} 93° to 94°C.; n _D ²⁵ = 1.4875)	
N - (p - dodecylphenyl) - 2,6 - dimethylmorpholine (b.p. ₂ 206° to 207°C.)	
N - cyclododecyl - 2,6 - dimethylmorpholine (b.p. _{1.5} 161° to 162°C.)	65
4 - tridecylmorpholine (b.p. ₁ 152° to 156°C.)	
4 - tridecyl - 2 - methyl - 6 - ethylmorpholine (b.p. _{0.2} 136° to 137°C.; n _D ²⁵ = 1.4566)	70
4 - tridecyl - 3,3,6 - trimethylmorpholine (b.p. _{0.3} 121° to 123°C.; n _D ²⁵ = 1.4573)	
4 - tridecyl - 2 - methyl - 5,5 - dimethylmorpholine (b.p. _{0.3} 125° to 129°C.; n _D ²⁵ = 1.4520)	
4 - tridecyl - 3,3 - dimethylmorpholine (b.p. _{0.1} 111° to 112°C.; n _D ²⁵ = 1.4607)	75
4 - cyclooctylmorpholine hydrochloride (m.p. 216° to 217°C.)	
2,2 - dimethyl - 4 - cyclooctylmorpholine hydrochloride (m.p. 188° to 189°C.)	
2,6 - diethyl - 4 - cyclooctylmorpholine hydrochloride (m.p. 165° to 166°C.)	80
2 - methyl - 4 - cyclooctylmorpholine hydrochloride (m.p. 177° to 178°C.)	

The fungicidally and/or fungistatically active agents according to this invention may be made up into dusting powders in the usual way by adding inert pulverulent carriers or diluents or may be made up by the addition of inert dispersing agents, wetting agents and/or adhesives, to solid or liquid compositions for the production of sprays. It is also possible to use the substances according to this invention as emulsions or solutions which may be sprayed by the aerosol method. Admixture with other fungicides and/or insecticides is also possible. The compounds according to this invention are especially effective with true mildew fungi, (for example Erysiphe), but are also effective with other injurious fungi, for example Botrytis cinerea.

Insofar as the compounds according to this invention have systemic action, they may also be used as seed dressings.

The invention is illustrated by the following Examples but not limited thereto.

EXAMPLE 1

Leaves of barley seedlings growing in pots are sprayed with aqueous emulsions of 80% of active substance and 20% of emulsifying agent and after the sprayed coating has dried the leaves are dusted with spores of barley mildew (*Erysiphe graminis* var. *hordei*). The test plants are then placed in a greenhouse at temperatures between 20° and 22°C. and at 75 to 80% relative humidity. The scale of mildew fungus development is determined after 10 days. The results observed are shown in the following table. The active substances tested are shown in the first column, namely 2,6 - dimethyl - 4 - tridecylmorpholine (A)x, N - cyclooctyl - 2,6 - dimethyl-

5 morpholine hydrochloride (B), 2,6 - di - methyl - 4 - tridecylmorpholine formate x (C), acetate (D), butyrate (E), acrylate (F), crotonate (G), oxalate (H), malate (I), adipate (J), maleate (K), lactate (L), tartrate (M), citrate (N), ethyl hexanate (P), 2,4-dinitro - 6 - (methylheptyl) - phenyl crotonate (comparative compound) (Q), untreated control (R). The remaining columns (headed "Attack") give the attack on the leaves after they have been sprayed with liquors containing the stated percentage of active substance; the extent of the attack is represented by the integers 0 to 5, 0 indicating no attack and 5 indicating total attack; the sign + indicates slight damage to the leaves.

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Active substance	Attack								
	0.0035%	0.0075%	0.015%	0.06%	0.03%	0.5%	0.1%	0.2%	0.12%
A	0	0	0		0				
B		2	1		0	0	0	0	
C	0	0		0+	0				0+
D	0	0		0	0				0+
E	0	0		0+	0				—
F	2	1		0+	0				—
G	1	0		—	0+				—
H	0	0		0+	0				—
I	1	0		0	0				0+
J	0	0		0	0				0+
K	0	0		0+	0				—
L	0	0		0+	0+				—
M	1	0		—	0+				—
N	1	0		—	0+				—
P	0	0		—	0+				—
Q	5	4	1		0				
R		5			5				

Active substance	Attack on leaves after spraying with liquor containing the percentage stated of active substance			
	+ = 0.0035	0.0075	0.015	0.03
4-p-/o-dodecylphenyl-2,6-dimethyl-morpholine	x 3	2	1	0
4-cyclododecyl-2,6-dimethyl-morpholine	1	0	0	0
4-tridecyl-2,2,6,6-tetramethyl-morpholine	x —	1	0	0
4-tridecyl-2,6-diethyl-morpholine	x 0	0	0+	—
4-tridecyl-2-methyl-6-ethyl-morpholine	0	0	0+	—
4-tridecyl-2,5-dimethyl-morpholine	2	2	1	0
4-tridecyl-3,3,6-trimethyl-morpholine	1	1	0	0+
4-cyclooctyl-2,6-dimethyl-morpholine-benzoate	—	1	0	0
4-tridecyl-3,3-dimethyl-morpholine	x 0	0	0	0
comparative compound: 2,4-di-nitro-6-(methyl-heptyl)-phenyl-crotonate	5	4	1	0
control (untreated)	5	5	5	5

x = isomeric mixture (with reference to alkyl or alkylaryl radical)

EXAMPLE 2

Leaves strongly attacked by true mildew (*Uncinula necator*) of grapevines planted in pots are sprayed with aqueous emulsions of 80% of active substance and 20% of emulsifying agent. The test vines are then placed in a greenhouse in diffused light in a chamber with high humidity and a temperature of 20° to 22°C. After a fortnight the coating of mildew on the leaves is evaluated according to the following scale:

0=mildew fungus destroyed

1)= more or less marked destruction of the
2)= considerable white mildew coating on
the leaves (no curative action of the
active substance).

3)
4)= extent of further development of the
fungus

5) = considerable white mildew coating on
the leaves (no curative action of the
active substance).

The following table indicates the results, the first column giving the name of the active substance used and the remaining columns giving the attack pattern on the leaves after they have been sprayed with a liquor containing the stated percentage of active substance:

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Active substance	0.0016%	0.0035%	0.0075%	0.015%	0.03%
2,5-dimethyl-4-tridecylmorpholine	1	0	0	0	0
2,4-dinitro-6-(methyl-heptyl)-phenyl crotonate (comparative substance)	5	4	2	0	0
control (untreated)	5				

EXAMPLE 3

5 Cyclamen plants are sprayed with aqueous emulsions of 80% of active substance and 20% of emulsifying agent and after the sprayed coating has dried out the plants are infected with a spore suspension of grey mould (Botrytis cinerea). The test plants are then placed in a chamber with very high humidity and temperatures between 20° and 25°C.

10 After three weeks, the extent of the development of the grey mould is determined and evaluated according to a scale graded from 0 to 5, 0 indicating no attack and 5 indicating the extent of the attack of untreated control plants. In the following table an active substance (2,6 - dimethyl - 4 - tridecylmorpholine) is compared with an untreated control. Attack after the plants have been sprayed with liquors containing the stated percentages of active substance is shown in the table:

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	0.0035%	0.0075%	0.015%	0.03%
active substance	4	2	1—0	0
control		5		

WHAT WE CLAIM IS:—

1. Any compound having the general formula

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$$\begin{array}{c} R_1 - N \backslash / \\ \quad R_2 - R_3 \\ \quad \quad \quad / \\ \quad R_4 - R_5 \quad \backslash \\ \quad \quad \quad O \end{array}$$

30 or a salt or molecular or addition compound thereof, in which R_1 denotes a cycloalkyl radical with more than 6 annular carbon atoms or a tridecyl or an alkyl - phenyl radical, R_2 , R_3 , R_4 and R_5 may be identical or different, each denoting an unsubstituted or substituted methylene radical, the substituents being one or two methyl- and/or ethyl- and/or phenyl groups.

35 2. The compound 4 - tridecyl - 2,6 - dimethylmorpholine.

3. The compound 4 - cyclooctyl - 2,6 - dimethylmorpholine.

4. The compound 4 - cyclododecyl - 2,6 - dimethylmorpholine.

5. The process for the production of compounds as claimed in claim 1, substantially as herein described.

6. Any fungicidal composition which contains a compound as claimed in claim 1, and an inert carrier or diluent.

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